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IMMUNE STATUS CHANGE THROUGH VACCINE RECIPIENT

ISHRAT JAHAN & MOAMMAR HOSSAIN

Department of Biotechnology and Genetic Engineering, Mawlana Bhashani Science and Technology University, Tangail, Bangladesh

ABSTRACT

Vaccines, it's a kind of biological preparations which is artificial. Vaccines will be used to maintain immunity of a specific disease. There are different types of vaccine discovered from the Jenners live, attenuated vaccine to DNA vaccine. Vaccination and immunization are closely related to each other. Human immune system can produce unlimited variety of different antibodies that response to the antigens (vaccines). Different types of vaccines produce different mechanism inside the body. Influenza vaccine is one of them which produce different immune mechanism into the body and induce the body's immune system. However, vaccines have a great role in the body's defense system.

KEYWORDS: Vaccine, Biological Preparation, DNA Vaccine, Immunity, Antigen, Antibody, Immune System

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Original Article

INTRODUCTION

Definition of Vaccine

Vaccines, it's a kind of biological preparations which is artificial. Vaccines will be used to maintain immunity of a specific disease. A vaccine normally carries an agent that looks like same as disease-causing microorganism. Sometimes it's created by weakened or killed forms of the microbe, it's sometimes may be toxin or surface protein. The vaccine stimulates the body's immune system to recognize the foreign particle then destroy remember it, so that the body's defense system can easily identify and destroy same types of microorganisms (1).

V*accine* is common term nowadays derives after Edward Jenner's *cow pox* diseases (Latin words variola vaccinia, came from the Latin word vaccīnus, sometimes it's thought it came from vacca which means cow), that used to provide protection from smallpox. The most common method of administering vaccines is by injection but some are given by oral or nasal spray (2).

Difference between Vaccination and Immunization

The difference between vaccination and immunization is listed below.

Table 1

Vaccination	Immunization
Vaccination is an inoculation with any vaccine or toxoid to establish resistance to a specific infectious disease.	Immunization is the process by which an individual's immune system becomes fortified against an agent
Vaccination is an individual event.	Immunization refers to a population.
Vaccine may be intact but inactivated (non-infective) or attenuated (with reduced infectivity) forms of the causative pathogens, or purified components of the pathogen.	The most important elements of the immune system that are improved by immunization are the T cells, B cells, and the antibodies B cells produce
Vaccination' is an 'Active Immunization	Immunization could be both-Active and

	Passive'
Table 1: Contd.,	
Vaccination is done by using different pathogens	Immunization is done through various techniques, most commonly vaccination.

(3, 4)

Roles of Vaccine in Conferring Immunity

A stunning protection mechanism inside the body named immune system. Its main function is to provide defence against millions of microorganisms including viruses, bacteria. This immune system is not fully protected against the pathogens after born. Sometimes this immune systems need to improve by using vaccine or antigen like particle. As a result when non pathogenic organism or toxoid enters into the body, the body produces antibody against them which are essential for the real organism. However the main target of vaccination is to improve immunity against pathogenic organism. (4)

On the other hand it also said that vaccines are designed to stimulate the immune system to protect against microorganisms such as viruses. When a foreign substance invades the body, the immune system activates certain cells to destroy the invader. This activation of the immune system involves two main types of cells: B cells and T cells. B cells can able to make antibodies. T cells can be helper cells or killer cells. Helper T cells organize the immune response. Killer T cells attack cells infected by viruses. However vaccine increase immunity and it has a great role in conferring immunity (5)

History of Vaccination and Vaccine

In 1796 vaccines and immunization history were begun with the story of a country doctor who lived in England (Berkeley). His name is Edward Jenner. He is the performer of world's first vaccination (6). James Phipps, an eight-year-old boy was inoculated with pus from a cowpox lesion. After, six weeks later Edward Jenner noticed that the boy, James Phipps was unaffected (7). On the basis of twelve experiments and sixteen case reports Jenner collected upto 1770s he concluded the vaccinology theory. After, such types of experiments were published by him as a classic text journal in that time. However, he concluded his works as the cowpox protects human from smallpox infection. Actually he is the pioneer of modern vaccinology (8).

Passive and Active Immunity

Types of Immunity is given through flow chart (3)

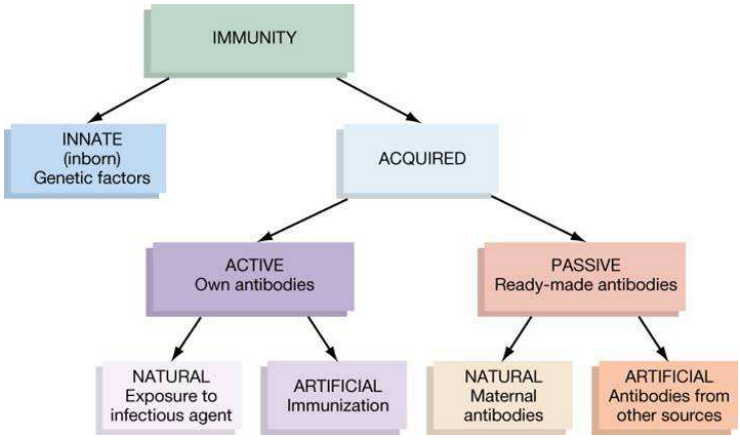

Figure 1

Passive Immunity

In passive immunity, antibodies have a great role to protect the diseased person or animal which is produced from other human being or animal. Passive immunity is a natural process. For example, new born baby got the maternal antibodies from its mother for protection, these antibodies passes through the placenta to fetus. In the passive immunity, large amount of antibodies are passes to the non-immune individuals which are specific for pathogen. This type of immunization showed when the time is not enough to develop a own immune response of an individual. Moreover it showed when the risk of infection is high (3).

Passive immunity is also two types,

- Naturally acquired passive immunity.
- Artificially acquired passive immunity.
- **Naturally acquired passive immunity**

Maternal immunity may be a sort of naturally acquired passive immunity, it refers to antibody mediated immunity carried to a fetus by mother during pregnancy. Maternal antibodies are passed through the placenta to the fetus by a receptor called FcRn found on the placental cells. It happens around the third month of gestation. Only antibody isotype called immunoglobulin G which can pass through the placenta (3).

- **Artificially acquired passive immunity**

Artificially acquired passive immunity is a limited immunization accomplished by antibody transfer, which can be executed as many types; as blood plasma or serum, as intramuscular use and as monoclonal antibodies (MAb). Passive transfer is operated prophylactically in the case of immunodeficiency diseases, for example hypogammaglobulinemia (3).

- **Active Immunity**

Active immunity, it's a kind of immunity specify the production of antibodies against a particular disease by the immune system. When B cells and T cells are activated by a pathogen, memory B-cells and T- cells develop. The main characteristics of memory cells is to remember each particular pathogen encountered all around the life of an animal, and create strong response if the same pathogen is recognized again.

There are two type of active immunity as like as passive immunity, which are

- Naturally acquired active immunity.
- Artificially acquired active immunity (5).

TYPES OF VACCINE

Vaccines are derived from different microorganism strain. Basically they are derived from the virus or from viral like agent. Different types of vaccine derived from different virus. However the traditional vaccine which derived from virus may be died or live, attenuated viral vaccine. Bacteria, fungus are not the source of vaccine because they contain huge amount of gene. These huge genes are the main obstacles for bacterial vaccine development.

There are many approaches to designing vaccines against microbe .On the basis of fundamental information about the microbe the following choices occurred, such as its infection and respond process to immune system, also the practical consideration such as region where the vaccine would be used. However following types of vaccines are found all over the world.

- Inactivated vaccine (9,10)
- Live, attenuated vaccine (9,10)
- Subunit vaccine (9,10)
- Conjugate vaccine (9,10)
- Toxoid vaccine (9,10)
- DNA vaccine (9,10)
- Recombinant vector vaccine (9,10)

MECHANISM OF VACCINE ACTIONS IN HUMAN BODY

Control or elimination of disease is needed the induction of protective immunity in an adequate proportion of the population. This is the best achievement by immunization programs which inducing long-term protection, a hallmark of adaptive immunity that differences to the fast moving but short-lasting innate immune responses. Long-term immunity is deliberated by the maintenance of antigen specific immune effectors or by the initiation of immune memory cells that may be adequately efficient and rapidly reactivated into immune effectors in case of pathogen exposure. B lymphocytes generate immune effector which are antibodies and able of attach exactly to a toxin or a pathogen (11). Another effector named cytotoxic CD8+ T lymphocytes (CTL) which may confine the spread of infectious agents by identifying and destroying infected cells or secreting specific antiviral cytokines. The production and maintenance of both B and CD8+ T cell responses is buttressed by growth factors and signals supplied by CD4+ T helper (Th) lymphocytes, which are divided into T helper 1 (Th1) and T helper 2 (Th2) subtypes. These effectors are guarded by regulatory T cells (T-reg) that are involved in maintaining immune tolerance (12). Most of the antigens and vaccines trigger both B and T cell responses. Furthermore, CD4+ T cells are essential for most antibody responses, while antibodies exert meaningful influences on T cell responses to intracellular pathogens (13).

Primary Response to a Vaccine

Primary response is done through the following sequential steps.

- First of all vaccinated against a particular disease where vaccine contains dead or weakened form of the organism.
- Even if the organisms are inactivated so that they are not able to make disease, they retain the properties of antigen which encourage producing antibodies against that organism.
- In the vaccine, the antigens are detected by the B lymphocytes when it’s on the organisms surface.
- The clone of identical cells are formed after the multiplication of B lymphocytes.
- Afterwards cloned B lymphocytes can be plasma cells or memory B cells.

- Antibodies are secreted by plasma cells. This antibodies are binding to the bacterium or viruses and disable their activity. (3)

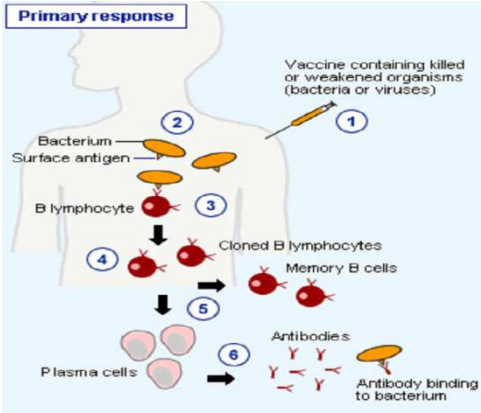

Figure 2: Primary response to a vaccine

Secondary Response to an Infection Primed by Vaccine

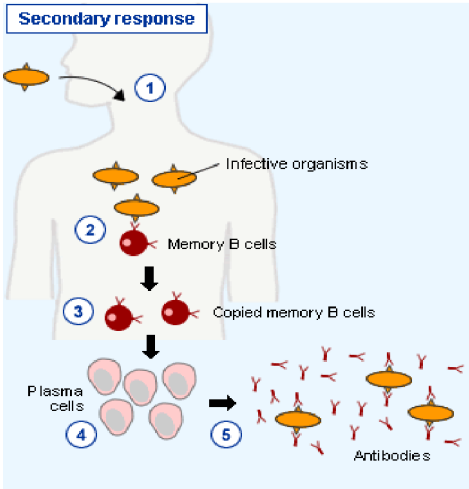

Figure 3: Secondary Response to a Vaccine

- Body exposed to the real infective organism.
- The organism is instantly recognized by the memory B cells that have lain dormant in the body.
- The memory B cells multiply rapidly.
- The memory B cells then develop into plasma cells (3).

Effectors Mechanism Triggered by Vaccines

- By extra and intracellular agents, antibodies can prevent or decline infections and clear extracellular pathogens by:
  - Joining to enzymatic active sites of toxins or preventing their diffusion.
  - Counterbalancing viral replication, e.g. preventing viral binding and entry into cells.

- Encourage opsonophagocytosis of extracellular bacteria, i.e. enhancing clearance by macrophages and neutrophils.
- Complement cascade activating.

- 2. CD8+ T cells do not block but decline, control and clear intracellular pathogens by:
  - Directly destroy infected cells by the release of perforin, granzyme, etc.
  - Indirectly destroy infected cells by antimicrobial cytokine release.
- 3. CD4+ T cells do not block but participate to decline, control and clearance of extra- and intracellular pathogens by:
  - Generating IFN-γ, TNF-α/-β, IL-2 and IL-3 and supporting activation and differentiation of B cells, CD8+T cells and macrophages (Th1cells).
  - Generating IL-4, IL-5, IL-13, IL-6 and IL-10 and supporting B cell activation and differentiation (Th2 cells) (5).

Molecular Mechanism of Influenza Vaccine

Influenza virus, a respiratory pathogen existing to the family Orthomyxoviridae (from Greek myxa, meaning 'mucus') (14). There are currently outlined three different types of influenza virus (A, B and C) which are illustrious by antigenic characteristics in two of their internal proteins, nucleoprotein (NP) and matrix protein (M). The three types of virus also vary in their pathogenicity and genome organization. Type A is found in warm blooded animals (birds and mammals), whereas types B and C are human pathogens. Most commonly cause human diseases are affected by Influenza A and B viruses which are two types. Based on the surface antigens influenza A viruses are subdivided into different subtypes, haemagglutinin (HA) and neuraminidase (NA). Now a days, 15 subtypes of HA (H1–H15) and nine subtypes of NA (N1–N9) have been discovered in influenza A viruses, and all subtypes are discovered in aquatic birds.

Influenza is always in process antigenic changes to get rid of the host's acquired immunity by two mechanisms: antigenic drift and antigenic shift. Antigenic drift is the aggregation of mutations in all influenza gene segments, but the changes are distinctly important in the surface glycoproteins (HA and NA). Point mutations are induced by the inherent error rate of the RNA-dependent polymerase complex, which absences proofreading ability. Influenza vaccine has been redeveloped almost every year to change viral activity. The antigenic drift of Influenza Avirus is more than influenza B. On the other hand, antigenic shift is infrequent and unpredictable for the viruses. It assumed that the lower animals such as birds, pigs are the source of influenza A virus.One more fact is disappeared virus is altered always by a new subtypes with novel glycoproteins (15). Genetic reassortment is the results of antigenic shift.

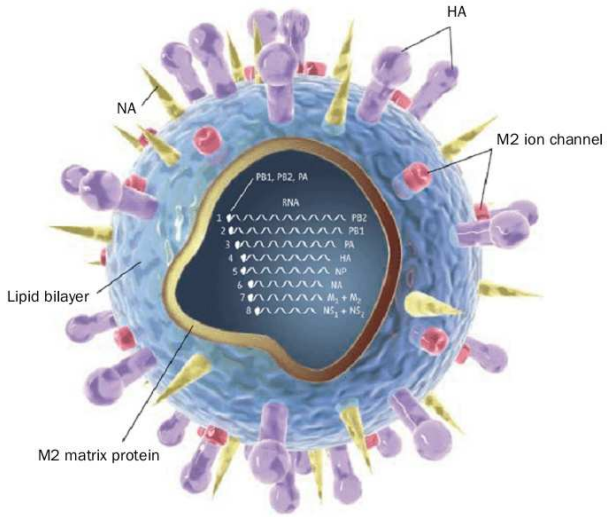

Figure 4: Structure of the Influenza Virus

The 8 gene segments are contained within a viral envelope with hemagglutinin (HA) and neuraminidase (NA) forming most of the antigenic determinants. The portion of the matrix 2 (M2) protein that is outside the viral envelope is antigenic (16).

PA = Polymerase Acidic;

PB = Polymerase Basic.

The best preventative measure against influenza is vaccination, and acts by developing neutralizes Abs directed against the HA, the major surface glycoprotein (17). Recently trivalent seasonal influenza vaccines involve antigen from two circulating influenza type a strains and type B strain.

Molecular Mechanism after Vaccination

- **Immune Response to Trivalent Inactivated Vaccine**

Both local and systemic responses are results by vaccination with intra venous (IV). As soon as 2–6 days after vaccination, develops in the serum antibody response to trivalent IV (TIV) can be detected (18). After vaccination, within two weeks 90% of vaccines have defensive antibody titres. Childrens of 6 months can establish defensive antibody levels after vaccination. The antibody reaction peaks 2–3 weeks after vaccination in primed subjects, and then diminishess over time and is generally two fold lower by 6 months' after vaccination (19). The serum antibody feedback is controlled by influenza-specific IgG antibodies (particularly IgG1) with minimum concentrations of IgM and IgA antibodies. Antibody persuaded after vaccination is type specific but can be largely cross-reactive, providing cross-protection towards earlier and newer viral strains. For the split-virus, vaccine encourages highest immune response towards the surface virus glycol proteins (HA and NA); in few cases, antibodies are stimulated towards internal viral proteins (20). After TIV in the tonsils, local immune responses are persuaded (a respiratory secondary lymphatic organ) and in the salivary or oral fluid (21). Predominantly, IgG and IgA influenza specific antibody-secreting cells (ASCs) were identified in peripheral blood tissue and tonsillar tissue after vaccination (22). In oral fluid, SIgA1 governed the antibody feedback with lower titers of SIgA2 (23). Juvenile diabetics had an equally very quick secured immune response after TIV in healthy individuals, but more studies are necessary to confirm the findings in another groups. In young children, the systemic immune response was

governed by IgM (which peaked later than IgG in adults), with a reduced systemic IgA response and no or very little SIgA discovered in the saliva. The primary status is crucial for the subclass of IgG and IgA produced (24). Currently, investigated a high basal level of influenza-specific ASC in the nasal mucosa, but this level is not affected by vaccination with TIV. For healthy subjects, hospitalization with the antiviral did not change the kinetics of the immune response to parenteral influenza vaccination (25).

- **Antibody and cell-Mediated Immune Responses to Influenza Vaccine**

Humoral and cell-mediated immunity are resulted by the stimulation of influenza virus which leading to an antiviral response in B and T lymphocytes continuously. Cytokine mediators activate viral T cells, trigger B-cells to make a distinction and outcome antibodies for a specific strain of a vaccine. These particular antibodies attach to exterior glycol proteins, hemagglutinin (HA) and neuraminidase (NA), to deactivate the virus element. To incorporate the forecasted spinning strains of influenza A/H3N2 and A/ H1N1 and influenza B, influenza vaccine required to be modernized every year. Antibody reactions to influenza vaccination have largely been estimated by the hemagglutination inhibition (HI) analyze. While the HI test is suitable and judged a gold standard, virus deactivation assays are getting more recognition as they are believed more functional. The antibody reaction to A/H3N2 strains is similar because the paradox narrated to HI titers regardless of the high illness trouble of influenza A/ H3N2 strains in adult contrast to juvenile adults. On the contrary, older adults are moderately secluded from H1N1 strains, at the same time as lower antibody titers to these strains in older contrasted to young adults have been scrutinized (26). These consequences will propose equivalent antibody-mediated defense aligned with A/H3N2 strains in two different types of adults, although keen dissimilarity to the watched products in grown-up adults; influenza A/H3N2 strains have maximum blow on hospitalization, compared to influenza B and A/H1N1 strains in inhabitants. Additionally, antibody response sometimes limited only for the repeated use of influenza vaccine, fortification in opposition to influenza develops while obtained yearly proposing to cellular immune systems may also significant for defense in the older adults. The mechanism in general turn down in vaccine-mediated safety in older adults has not so far started whereas antibody reactions to influenza vaccination have been showed a relationship with modifications in T-cell activity and a reduction in cell-mediated immune reaction to influenza vaccine (27).

CONCLUSIONS

The invention of vaccination was a turning point in the war between microbes and humans. Vaccines interfere with our immune system. The immune system is not strong by born, it needs to be stronger to invade the dangerous pathogens. However vaccination improves the immune system by different ways. Vaccine when enters inside the body it changes the body's immune status by the antibody-antigens reactions. The primary and the secondary responses are created through the vaccination, where bodies' immune system identifies the pathogens, as a results immune system can easily memories the same pathogens. Different types of cell such as T-cells, B-cells are also responsible for changing the immune status. However, later developments on characteristic safety bring advertised new insights over those components of vaccine-induced resistance and bring encouraged additional normal methodology to immunization configuration. On the other hand the molecular mechanism of vaccine is not only helped to know about the vaccine actions inside the body but also it helps to improve the vaccines too.

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